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Clinical Proceedings

OF THE CHILDREN'S HOSPITAL

WASHINGTON, D. C.

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PATHOGENIC E. COLI

Weekly Clinical Conference

E. Clarence Rice, M. D.*

INTRODUCTION

Evidence is now mounting that certain types of *Escherichia coli* induce diarrhea at least in infants.

The clinical laboratory facilities of a Children's Hospital should provide for making a diagnosis of *E. coli* serotypes related commonly to infantile diarrhea.

CASE REPORT

G. R. B., a 4½ year old white boy was admitted to Children's Hospital on January 28, 1956 with a chief complaint of vomiting and diarrhea of 12 hours duration. He had been asymptomatic until the day before admission when he began to have a frontal headache and a fever ranging from 102 to 106 degrees, both of which persisted through the night in spite of one 5-grain dose of aspirin. On the day of admission he vomited three times, passed four or five watery brown stools, was irritable, sleepy, and refused oral fluids.

The past and family histories were non-contributory.

When he was examined on admission, he was well developed and well nourished but quite lethargic. Except for enlarged, moderately erythematous tonsils and warm dry skin with fair turgor, physical examination was normal.

On admission the CO_2 combining power of his blood was 35 volumes percent, and therapy was begun with intravenous fluids, intravenous chloramphenicol, and oral aspirin. Blood culture, hemogram, urinalysis, and chest x-ray done at admission were all normal. Although the vomiting and diarrhea stopped after the first day of hospitalization, the patient remained febrile and listless for the next two days. Because of back pain on neck flexion, a lumbar puncture was performed and produced normal cerebrospinal fluid. At this point intramuscular procaine penicillin was given. The stool culture obtained at admission was then reported as showing growth of *E. coli* type O*127*, and the antibiotic regime was changed to oral administration of neomycin and chloramphenicol. The subsequent course was uneventful and the patient was discharged without symptoms on February 3, 1956, two days after a stool culture had shown no growth of pathogens.

DISCUSSION

Dr. Rice:

All of us are familiar with the common variety of *Bacillus coli* as we used to know it or *Bacterium coli*, or *Escherichia coli* as it is now called. This was one of the first organisms to be studied thoroughly and is known to be a normal inhabitant of the gastro-intestinal tract. Some of you have

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been surprised every once in a while when you received a report that we have found this organism in the throat culture of an infant. As time went on, physicians who cared for young patients with their gastro-intestinal ailments wondered if this organism might not be responsible for some of the gastro-intestinal upsets which infants and children have. Of course we have long known that if *Bacterium coli* gets out of its normal habitat and into such a place as the urinary tract, the peritoneal cavity or the blood stream, it can cause considerable havoc, and even death, but there was nothing very much to prove whether or not this organism could cause a real disturbance in the gastro-intestinal tract. It was not until 1927 that Adam in Europe made certain observations which suggested to him that possibly there was some etiological relationship between *E. coli* and the diarrhea of infants.

Later on, Bray and others in Great Britain brought up the same possibility that certain *E. coli* might be a factor in causing diarrhea. This work was subsequently continued on the continent and has made a fairly good case for the pathogenicity of the group of organisms. There was very little work done in this country until about 1950, when observers in New York and Michigan made certain observations which tended to confirm the work that had been done in Europe. About this time a virus which caused diarrhea in calves was isolated by Light and Hodes from the stools of infants with diarrhea, and this was an additional etiological factor which had to be considered.

Investigation has shown that the different strains of *E. coli* number well over a hundred and they can be separated on the basis of serological and other reactions. At the present time a number of these serotypes are available for bacteriology laboratories and practically all children's hospitals carry out the isolation of these so-called pathogenic types. Our bacteriologist cultures material from the bowel for the pathogens, *Salmonella* and *Shigella*, and in addition plates the inoculum on eosin-methylene blue and on sorbitol agars which aids materially in the isolation of the so-called pathogenic *E. coli*. Our greater ability to isolate these organisms is due to improved technic and materials, and a greater interest and awareness of the situation. At the present time the examination of a diarrheal stool goes through a good deal more of a bacteriological process than it did five or six years ago. After culturing these organisms on these various media, the bacteriologist subcultures on a tube of sorbitol agar, and a suspension of the organisms under study is tested for agglutination with various immune sera. This enables one to make an exact identification of the specific bacterium.

At present we are equipped with a battery of immune sera which we use to identify the following serotypes of *E. coli*: O127; O111; O55; and O26.

There are many more of course, and we will probably add additional typing sera as our work progresses.

Since April 1955, the following organisms have been isolated from the routine bowel cultures, which includes a search for so-called pathogenic *Escherichia coli*:

Total Number Of Stool Cultures: 957

Isolation of:		
Salmonella sp.	40	4.2%
Shigella sp.	67	7.0%
E. coli:		
O127	98	12.1%
O111	8	
O55	5	
O26	4	

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B. COLI GASTROENTERITIS

JOURNAL CLUB REVIEW

Robert T. Scanlon, M.D.*

Pathogenic *Bacterium coli* (*Escherichia*) was first isolated and identified by Bray[1] in 1945 in a diarrhea epidemic of 51 cases with 20 deaths. He termed the organism *Bacterium coli neapolitanum* and defined it as the sucrose and salicin fermenting strain of *Bact. coli*. Giles and Sangster[2] isolated a strain which they termed α type *Bact. coli*; Taylor, et al[11] typed and labeled a strain of *Bact. coli* as D433. Finally, in 1947,[3] a second serologic type was isolated by Giles, Sangster and Smith and termed type β.

Additional study and serologic typing by Kauffmann resulted in a specific grouping and classification (Kauffman's). He found that Bray's

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Bact. coli neapolitanum, Giles' α type, and Taylor's D433 were all serologically identical and grouped them in O111. Giles type β was grouped in the O55 grouping. Kauffmann's classification was based on antigenic properties: O (somatic), K (capsular), and H (flagellar) antigen[4]. The following strains have all either been definitely implicated in epidemics or have been suspected in the causation of epidemics: O111, B4; O55, B5; O26, B6; O122A; B11, O112A; B7, O86; B14, O119; O125, B15; B16, O126; O127, B8.

Identification of organisms was based on colonial characteristics, biochemical traits and agglutination studies. Stock, et al, describe colonies of *E. coli O111, B4* as gray, nearly flat and non-hemolytic in type with regular margins as contrasted to the larger more irregular margins of nonpathogenic colonies of *E. coli*. Very characteristic of the O111, B4 is the seminal odor[1].

Identification of colonies was based on the typical appearance on Endo and MacConkey's media and blood agar [5, 6]. Charter and Taylor's type D433 grew out on Endo agar but did not grow adequately on SS agar and desoxycholate agar[6].

Various cultural reactions were described as being typical of *E. coli*. Neter, et al[5], described as being characteristic the presence of a particular INVG reaction, no H-S production and no decomposition of urea. Neter[5] also considers of importance the production of Indole, the presence of methyl red, the Voges-Proskauer reactions and the failure of growth in Koser's citrate solution.

Fermentation reactions of importance are fermentation of salicin and sucrose[1, 5] and the formation of acid and gas from glucose, lactose and sucrose.

Bray, et al[1], summarize the reactions for *Bacterium coli neapolitanum* in Chart I.

CHART I

Glucose	Maltose	Mannitol	Lactose	Sucrose	Salicin	Indole	Motility	V.P.	M.R.	Gelatin liquefy	Number of Strains
AG	SlA	AG	AG	AG	AG	+	−	−	+	−	45
AG	SlA	AG	−	AG	AG	+	−	−	+	−	10
AG	AG	AG	AG	AG	AG	+	−	−	+	+	2

A—Acid; G—Gas; Sl—Slight.

The organisms were found to be non-motile at 37° and motile at 22°C[6].

Agglutinin Tests

Rabbit anti sera containing the O and B antibodies were prepared as follows: To maintain both O and B antibodies, rabbits were immunized

with unheated O111, B4 organisms; to maintain only the "O" antibody, rabbits were immunized with organisms heated at 100° for 2 hours. Positive results are based on:

a) strong instant agglutination with "OB" serum.

b) slower agglutination in "O" serum.

Neter, et al[5], carried out an agglutination test at 50° C. Giles, et al[3], in 21 of 41 patients had agglutination titers as high as 1:640. However, Bernet[7] feels that attempts to demonstrate serum agglutinins and hemagglutinins have been successful in only some cases and the reaction is, therefore, not truly diagnostic; this procedure has not been widely used because of the instability of the antibody[7].

Finally, phage typing of O111, B4 organisms was performed[8]; the organisms were classed in phage type Series III; their flagellar antigens were identical.

Age, Prognosis

The majority of cases of illness due to "pathogenic" *E. coli* occurred in infants below one year of age. According to Rodgers[9] *E. coli* enteritis is usually a disease of the very young, from birth to 18 months. Bernet[7] in contrast to other studies found that his patients over three months of age did not have positive cultures or any signs of gastroenteritis when exposed to patients infected with organisms. Finally, it has been reported that *E. coli* does not cause diarrhea in adults but they can become carriers[7].

The occurrence of *E. coli* gastroenteritis (O111 and O55 strains) has been reported to be fatal in an average of 50.6 percent of cases[4].

Epidemiology

There have been many studies on possible modes of spread of *E. coli* to cause epidemic diarrhea in young infants. The obvious mode whereby an unsuspected infected child is put into a ward with normal children is often unavoidable. A study of this type of spread was reported by Stock, et al[10]. Here two children with *E. coli* diarrhea were unwittingly transferred to convalescent homes, wherein a series of small epidemics was started.

Similar studies were performed by Taylor and Powell[11], Taylor and Charters[12], Neter and Trussel[13], Neter and Schumway[17], Giles and Sangster[2], and Bray[1].

An interesting case study was done in Glasgow[15]. Three different wards were included in the study, each with various degrees of isolation technique. Ward A had the best isolation: single cubicles, a "dirty" nurse and a "clean" nurse, careful handling of laundry. Ward C was the other extreme due to a shortage of help: cubicles were not separated; there was only one nurse; and the only preventive was hand washing. Ward B's

technique was intermediate. Therefore, it would be expected that Ward A would have a decidedly lower infection rate than the other two wards, with Ward C having the worst record. However, this was not borne out. The rates for Wards A, B and C were 34 percent, 24 percent and 23 percent respectively. Of 113 patients, 67 percent developed symptoms and 5 died.

Alexander, et al[16], in 1952 studied 124 babies admitted to a cubicled ward for various reasons. All of these babies' feces were negative for *E. coli* pathogens. However, out of the 124 babies, 74 acquired *E. coli* O111 and 34 developed O55. An unstated number of babies was given antibiotic prophylactically but instead of preventing cross infection, this procedure seemed to aid cross infection by allowing the emergence of resistant strains.

Rodgers[9] postulated that it is not the nurses who spread the organisms but rather the ward articles that come in contact with the baby. This seems to be exemplified by the Glasgow study, and by a study of Rodgers[9]. This investigator cultured ward articles, air, dust and bed sheets. His main findings follow:

a) *E. coli* was obtained from the air almost immediately following the making of the beds;

b) All articles within a room were contaminated with *E. coli* within 18 hours after admission;

c) On one occasion the broom was washed with 5 percent lysol and hung out in the sun to dry; however, *E. coli* were not killed;

d) The cart used to take the children to x-ray was contaminated even after being washed with 5 percent lysol;

e) The weighing machine was always contaminated.

The indication seems to be that *E. coli* could be passed from room to room by any of the above articles.

It has been stated that *Salmonella* and *Shigella* organisms can be passed via air contamination from a throat carrier. Neter and Shumway[17] studied 40 patients, five of whom carried D433 in the stools. Of these five, two patients had the organism in the nasopharynx and one had it in the throat. These patients had not vomited so it is presumed that the organisms infected the nasopharynx and throat in another way. Bernet, et al[7], cultured *E. coli O127, B8* from the nose and throat of his patients. Laurel, et al[14], also postulated respiratory spread due to the presence of the *E. coli* organism in the nose and throat of their patients.

In addition a number of authors found that breast fed babies did not seem to contract the disease. Also, it has recently been shown that mothers had high levels of *E. coli* antibodies in their serum while the babies did not; therefore, it is postulated that the lack of infection in breast fed babies is due to the acquisition of antibodies from the mother via breast milk.

Do healthy individuals carry the organism? Bray found that 4 percent

of 100 individuals in contact with *E. coli* harbored the organism[1]. Giles, et al, in a study of 721 patients (supposedly normal) but in a hospital where E. coli was present, found that 1.8 percent had positive cultures[9]. Taylor, et al, however, found that 208 controls with no contact had negative cultures[9]. A similar result was obtained in a study of 108 children at Birmingham Hospital. Taylor and Charter[18] cultured 255 healthy controls and obtained only 3 positive stool cultures: *Bact. coli canioni*, Type E 611, and O Group 86.

Bernet[7] during an epidemic of *E. coli* cultured 455 patients from the general population of Denver. Of these, 327 had diarrhea, but only 2 babies grew out *E. coli O127 B8* in culture. These cultures were obtained at the same time that a hospital epidemic of *E. coli* was being managed by Bernet.

Is *Bact. coli* normally present in the bowel as it is in higher animals? Stevenson[19] in 1950 cultured 72 adult patients with diarrhea secondary to another condition, e.g., ulcerative colitis, mucous colitis, or carcinoma. Fourteen of these adults were positive for D433. Stevenson suggested that the organism may be present in the jejunum and in the above patients may have been washed down into the lower bowel.

However, J. Smith[18] has stated that he has repeatedly failed to isolate these organisms in cases of bacillary dysentery. In addition K. B. Rodgers[18] failed to isolate them at autopsy from the jejunum except in the presence of related symptomatic history.

Signs and Symptoms and Laboratory Findings

All epidemics were characterized by one or more of the following signs and symptoms: diarrhea, vomiting, dehydration, and lethargy.

Belnap[4] found that many of his patients had hyperelectrolytemia, shock and cyanosis. He noted that other authors have described cerebral phenomena in *E. coli* diarrhea patients but did not rule out hyperelectrolytemia. He postulates that convulsions were on the basis of hypernatremia. Belnap[4] also found that the shock was ameliorated approximately one hour after desoxycorticosterone acetate (2.5 cc/Kg) and Cortisone (6.25 mgm/Kg) were administered.

Treatment

Antibiotics are definitely indicated; the treatment of choice appears to be either chloramphenicol or neomycin, with a combination perhaps being more efficacious.

A combination of penicillin and streptomycin has no value at all; in fact resistant strains or new strains have appeared while this treatment was being used. Streptomycin alone appears to be of no value. This opinion of Rodgers agrees with Alexander, et al[16], and Neter and Shumway[17].

Alexander's conclusion was that there was no significant difference shown between the streptomycin treated series and the control series[16]. Severe relapses were slightly higher in streptomycin treatment cases.

Magnusson[20] in 1950 used chlortetracycline for 8 patients and obtained a good effect in all 8; after a few doses all stool cultures were negative. Neter and Shumway[17] in 1950 stated that chlortetracycline as well as oxytetracycline and chloramphenicol produced equally good results.

However, Stulberg, et al[21], in 1954 used chlortetracycline (10–15 mgm per lb per day) with no effect in their cases.

Chloramphenicol was recognized as an effective agent in 1949 when Rodgers and Gerrard[22] found that 14 out of 15 cases were cleared within 1–5 days of chloramphenicol therapy (75 mgm per lb per day). This drug was also recommended by Neter and Shumway[17]. Wheeler and Wainerman[23] in 1954 tried chloramphenicol or neomycin with the results as charted (Chart II). Out of 23 cases the organism in twelve became resistant to chloramphenicol while no cases were so reported with neomycin.

CHART II

	Chloramphenicol	Neomycin
	(*35 mgm/Kg/dy*)	(*50 mgm/Kg/dy*)
Number of patients	23	14
Fail to elim. in 4 days	4	0
Clinical regression	4	1
Cultured relapse	3	1
Unsuc. attempts at	7	—
Drug resistance	12	0
Deaths	0	0

Stulberg, et al[21], used neomycin (50–100 mgm/Kg/d) when chlortetracycline was ineffective, and the cultures were negative in 12–24 hours. Here 13 of 21 patients had bacteriologic recurrences while only two had clinical recurrences. One year later, Stulberg[24] found that neomycin sterilized the stool almost immediately but that *E. coli* commenced to reappear soon after cessation of treatment. The recommended dose of neomycin is 50–100 mgm/Kg/d[24, 25].

In vitro sensitivity studies of *E. coli O127: B8* showed that the most effective drugs in order are polymyxin, neomycin, chloramphenicol, tetracycline and oxytetracycline. All strains were resistant to dihydrostreptomycin and sulfadiazine[26].

Finally, Belnap[4] raises the possibility that hyperimmune serum may be more effective than the antibiotics.

In summary, it may be stated that *E. coli* gastroenteritis is for the most part a disease of the young (0–18 months) with its highest mortality in

infancy. Chloramphenicol and neomycin used concomitantly appear to be the most effective antibiotic treatment.

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DIAGNOSIS AND TREATMENT OF CONGENITAL HEART DISEASE

John O. Nestor, M.D.*
Bernard Walsh, M.D.†
George Courie, M.D.‡

We are presenting two cardiac problems which were selected primarily to show the members of the medical staff the type of work we are attempting to do in the Cardiovascular Clinic at Children's Hospital, and not particularly because they are interesting cases. We would like to illustrate our con-

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servative attitude toward diagnostic procedures and surgery for children. I think these will point out that we have attempted to let time make the diagnosis for us as long as it did not increase the risk to the patient. We followed the first case, C. P. who is now 7 years of age, for several years. We first saw her when she was 1 year of age. We followed the second case, L. M., who is now 4 years of age, since he was 1 year of age. I think that will illustrate our attitude; we feel that we should procrastinate before doing special diagnostic procedures or surgery except in those patients who seem likely to develop permanent and irreversible pulmonary changes as a result of delay. We would also like to illustrate the problems inherent in making a decision concerning surgery in this day of rapid advances, for surgical changes are so common that one procedure hardly gets into the literature before the next one is attempted. The question of what to do in some cases will be answered in the second of the cases to be presented.

CASE NO. 1

C. P., a 7 year old white girl, was a premature baby weighing 4 pounds, 8 ounces at birth. When first seen in the Out Patient Department at 13 months of age she weighed only 17 pounds, 13 ounces, and could do nothing more than sit up alone. At that time the heart was large; there was a systolic precordial thrill; and a loud harsh systolic murmur loudest in the pulmonary area could be heard. By January 1950, at 2½ years of age, she had been sick most of her life either with diarrhea or respiratory infection. A three-lead electrocardiogram showed only a right axis deviation, and fluoroscopic examination revealed vigorously pulsating pulmonary arteries. A well-heard split pulmonary second sound and the previously described systolic murmur and thrill in the pulmonary area were present on physical examination. When seen again in April 1951 at 3 years and 9 months of age, she was still having frequent respiratory infections and not eating well.

She was seen in April 1954 when 6 years and 9 months of age, and was doing much better in that she was having only occasional respiratory infections; she was eating well, and her activity was unlimited. The physical findings were essentially unchanged, and the electrocardiogram revealed a right axis deviation, vertical heart, and right ventricular hypertrophy. Fluoroscopy revealed a slightly convex main pulmonary artery segment and no mention was made of the hilar pulsation previously seen.

Cardiac catheterization was performed on March 29, 1955 and arterial blood under low pressure was obtained from the right pulmonary artery. This was not a wedge sample. The right ventricular pressure was three times normal and there was no evidence of a shunt within the heart.

Because the catheterization findings suggested the presence of a pulmonary arterio-venous fistula, an angiocardiogram was done. Twelve x-rays films taken in AP view at ½ second intervals were not revealing. Twelve x-ray films taken in the right oblique view at ¾ second intervals revealed a pooling of the dye in a branch of the right pulmonary artery and refilling of this area from the aorta when the latter filled with dye (Figure 1). This was thought to be a pulmonary arterio-venous fistula involving a bronchial artery.

On May 12, 1955, at 7 years and 10 months of age she was well developed and well

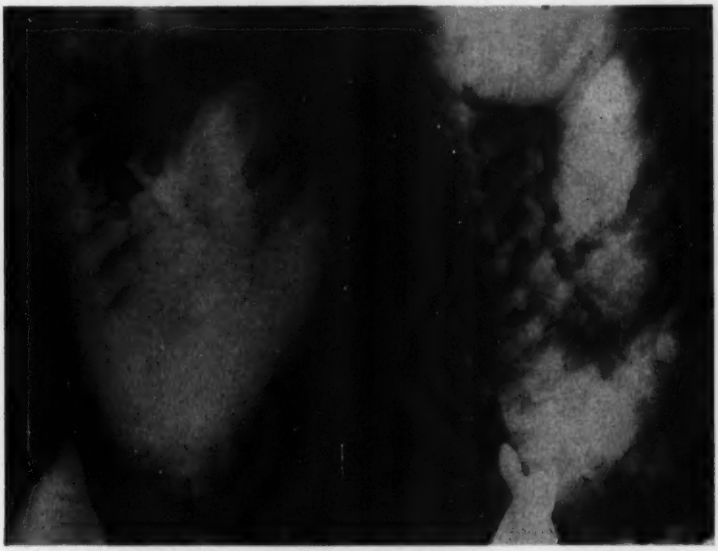

FIG. 1A & 1B. Case No. 1. Right posterior oblique x-ray views of the heart and great vessels taken following the injection of dye.

1A—Film #9. Six and three-quarter seconds after injection. The aorta is beginning to fill.

1B—Film #10. Seven and one-half seconds after injection. Both aorta and right pulmonary artery are filling.

nourished. There was no cyanosis, dyspnea, or exercise intolerance. The systolic murmur and thrill were unchanged. On fluoroscopy there was an enlarged heart, a left aortic arch, a convex main pulmonary artery segment, and prominent right hilar vessels, but no definite pulsation. The ventricles were slightly enlarged but the left auricle was normal.

DISCUSSION

Dr. Nestor:

Until we catheterized this girl we had no suspicion and no evidence to indicate that there was extra-cardiac pathology. The catheter was advanced with ease into the right main pulmonary artery and then out to the mid-right lung field where much to our surprise, we obtained light red arterial blood under a pressure of 15/9 mm of mercury. The catheter was drawn back into the right main pulmonary artery where venous blood under a pressure of 25/17 mm of mercury was obtained. This procedure was repeated a total of 3 times proving that we were not getting a wedge pressure in the mid-right lung field. The completed catheterization revealed a

pressure of 75/0 in the right ventricle and no step-up in oxygen content of the blood in the right heart, thus indicating the presence of a pulmonary stenosis without an intra-cardiac shunt. Analysis of the sample taken in the right pulmonary artery revealed a step-up in oxygen content of more than 5 volumes percent over the sample taken in the mid-right lung field.

Although the standard x-ray films revealed no evidence of a pulmonary-arteriovenous fistula we were forced to conclude that she had one in addition to pulmonary stenosis and we felt that we should be able to prove it by angiocardiography.

Films taken in the anterior posterior view at ½ second intervals after the injection of the opaque medium did not reveal any definite evidence of a fistula. Because the aorta was just beginning to be visualized on the twelfth film, at the end of six seconds, we then changed the interval to three-fourths second for the repeat in the right posterior oblique position. On an early film of this second series a puddle of dye was seen to form in the region of the right descending pulmonary artery branch. The tenth film in the oblique position at 7½ seconds after the start of injection revealed strikingly how a branch of the right pulmonary artery filled as the aorta filled with the dye, seeming to prove that there was a pulmonary arteriovenous fistula involving a bronchial artery. To be absolutely certain, at a later date, we attempted to perform an aortagram but were unsuccessful. Of course the angiocardiogram also confirmed the presence of pulmonary stenosis.

Thus we have a seven year old girl who, although she did poorly during the first four years of her life when her growth and development were delayed and she had repeated respiratory infection, is now well developed and entirely without symptoms of any kind. She is not cyanotic or dyspneic and there is no diastolic murmur. She has only the systolic murmur of the pulmonary stenosis, yet she seems also to have an unusual type of pulmonary arteriovenous fistula filling from a branch of the aorta.

Dr. Walsh:

This case illustrates a number of very interesting points. When we first saw this child and, in fact, until quite recently, we considered her to have an interatrial defect. However, she has had a pretty well-defined split pulmonary second sound and a grade three to four systolic murmur with an accompanying systolic thrill. Patients with interatrial defects as a rule do not have such a murmur and thrill. The split pulmonary second sound was quite persuasive, so that when she was catheterized we were somewhat unprepared to find the differential pressure between her right ventricle and her pulmonary artery to show she had pulmonary stenosis, though not marked in degree.

Those excellent angiocardiograms were almost diagnostic of pure pulmonary stenosis. In pure pulmonary stenosis the dye will hold up in the right ventricle, and will stay there well beyond the usual time. The main pulmonary artery stays filled even when the dye fills the aorta producing the appearance of a large button or coin.

The extraordinary finding on catheterization was the high oxygen saturation well out in the right lung. The usual pulmonary arteriovenous fistula is a communication between a pulmonary artery and a pulmonary vein in the lung. As a rule the greatly increased amount of collateral circulation about a fistula is readily seen in angiocardiographic study but such is not so here. This is in keeping with the repeated findings on catheterization, indicating a direct communication between a pulmonary and a bronchial artery. Such a communication is probably of little significance, or at least is doing no apparent harm now.

The degree of pulmonary stenosis here is not great and perhaps this accounts at least in part for the presence of a well split pulmonary second sound. The finding of the systolic pressure in the right ventricle to be 75 mm., a figure three times the normal level, is what we have been finding on catheterization in a very few patients with pulmonary stenosis who, like this child, are having no limitation of exercise tolerance and are getting along about as well as their normal contemporaries. We cannot exclude the opinion that the narrowing of the pulmonary outflow tract in this child is not valvular but rather sub-valvular in the infundibulum. There is no completely reliable method of making the distinction between valvular and infundibular obstruction in these patients short of surgical exploration. It has been our practice in the past two years to recommend pulmonary valvulotomy for those whose systolic pressure in the right ventricle was 100 mm. or more, and for those with less than that to wait for two or three years and recatheterize them. If we could be sure that the stenosis was infundibular rather than valvular I believe all of us in the Cardiac Department would feel that such a child should not be treated surgically at this time as we believe the surgical treatment for such a defect is not, as yet, sufficiently well established.

CASE NO. 2*

L. M., a white boy, 3 years and 8 months of age, was seen first at the age of 1 year. He was described as apparently normal at birth, but at 2 months of age a heart murmur was detected. At 6 months of age, labored breathing was noted, following which he began to tire easily and became slightly cyanotic. At the age of 1 year, he had his first episode of acute anoxia and was hospitalized with complaints of dyspnea, cyanosis, and easy fatigue. His growth and development had been fairly normal up until

* Private case of Dr. George Maksim.

FIG. 2A. Case No. 2. Anterior Posterior x-ray view of the heart. The heart appears apparently normal in size and shape.

this time. Dentition began at 5 months of age, he sat alone at 6 months and stood alone at 11 months of age.

At 1 year of age he was an irritable child who was acyanotic at rest but became cyanotic when crying. He appeared well developed and well nourished. There was no chest deformity. A harsh systolic murmur was heard with maximum intensity in the third and fourth left interspace. There was no thrill or shock. P_2 was diminished in intensity. The liver and spleen were not enlarged.

Electrocardiogram revealed right axis deviation and a vertical heart but no definite evidence of right ventricular hypertrophy. Blood hemoglobin was 12.8 grams per 100 ml and hematocrit 44 per cent. X-rays of the heart and lungs were considered to be within normal limits. (Figure 2A).

He was re-admitted to the hospital at 2½ years of age and just recently at 3 years and 8 months of age, again with the complaints of episodes of severe dyspnea and cyanosis. These episodes appeared to be increasing in intensity and severity. A recent electrocardiogram revealed definite evidence of right ventricular hypertrophy.

Cardiac catheterization was attempted but the catheter could not be advanced into the heart from either side. Angiocardiogram revealed simultaneous filling of the aorta and main pulmonary arteries 1 second after injection (Figure 2B).

DISCUSSION

Dr. Walsh:

Those of us who see children with congenital heart disease are often surprised to note how little cyanosis there may be in the presence of a well defined tetralogy of Fallot. Very occasionally a child who comes to be classified as having a severe tetralogy will, when quiet at rest, display very little abnormal blueness of the mucosa or nailbeds. There is one pa-

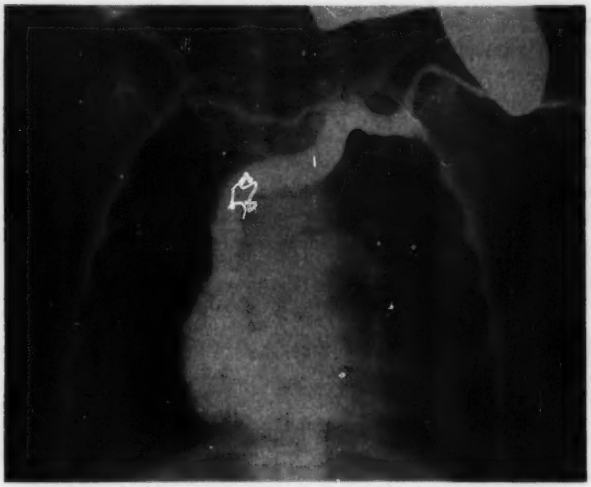

FIG. 2B. Case No. 2. Anterior posterior x-ray view of the angiocardiogram. This film was taken one second after completion of dye injection and reveals simultaneous filling of the aorta and pulmonary artery indicative of dextro position and overriding of the aorta.

tient in this hospital now who was operated on very successfully in the past week, a 13 year old girl with a moderately severe tetralogy who caused the house officers to doubt that she had any serious heart disease when they did not observe the degree of cyanosis they had expected.

This particular patient was chosen by Dr. Nestor today for discussion in order to bring out the views that are held today as to the proper surgical therapy for the treatment of a tetralogy. Until very recently the only question in these patients was when to operate since there was but one procedure to do, and that was the creation of an aorto-pulmonary shunt. In the continuing advances in the surgical therapy of congenital heart disease there is now a group of very competent surgeons who believe that the correct approach for a patient with tetralogy is the surgical removal of most of the obstruction in the pulmonary tract, whether that obstruction be in the infundibulum, pulmonary valve, or both areas. One variation which we ourselves have used here is, by the use of general hypothermia as anesthesia, to do a cardiotomy and remove the obstruction in the pulmonary tract under direct vision. Another group of surgeons now believe that it is worth attempting to correct completely the interventricular septal defect, the dextroposed aorta, and the pulmonary outflow obstruction in one procedure carried out under direct vision. A third group is working hard to perfect a mechanical extra-corporeal cardiac pump oxygenator

system which will permit the near total correction of the anatomical defects that these patients have.

While at a meeting in Atlantic City in the past two weeks I polled a panel of outstanding cardiac surgeons as to their method of dealing with such a patient as we have under discussion here. Two of the group were continuing the use of aorto-pulmonary shunts. Two were carrying out infundibulectomies. One, who has been the chief worker among the group attempting to perfect a pump oxygenator, was delaying operations on patients with tetralogy until the mechanical system was adequate.

TRAUMATIC PERIOSTITIS AND SUBDURAL HEMATOMA

Weekly Clinical Conference

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F. Burke, M.D.‡
J. Mateos, M.D.§
L. Rubio, M.D.‖
H. Stevens, M.D.¶

INTRODUCTION

A baby with periostitis and subdural hematoma is presented for discussion of the possible traumatic etiology of this syndrome.

CASE REPORT

This patient is a 2 month old colored girl who was admitted April 18, 1956 because of swelling of the right thigh and regurgitation since birth.

The infant is the first of twins born two weeks prematurely. One of the pair was delivered as a breech presentation, but which is not known. Her birth weight was 6 pounds, 8 ounces. Since birth the baby had had a seemingly painful and excruciatingly tender swelling of the right thigh. In addition she had regurgitated feedings excessively, and on occasion had projectile vomiting, although there was no difficulty in taking the formula. The history was not otherwise remarkable except that the patient's twin had recently died, and also has had regurgitation of its feedings.

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At the time of admission the patient was a poorly nourished colored infant who did not look ill, but who had scanty subcutaneous tissue. A slight degree of beading of the costochondral junctions was noted. The liver and spleen were barely palpable. The clitoris was enlarged. A tender, slightly hot swelling of the lower half of the right thigh extended over the right knee with limitation of motion at the joint. The right foot was likewise swollen, especially over the heel, and there was a talipes deformity. Physical and neurological examination were otherwise normal.

Laboratory results were as follows:

Hemoglobin 10.2 gms. per 100 ml., hematocrit 34 percent, WBC 11,600 with 43 percent polymorphonuclear forms, 1 percent bands, 46 percent lymphocytes, 8 percent monocytes, and 2 percent eosinophiles; urinanalysis normal; sickle cell preparation was negative; BUN 11.0 mg. per 100 ml., potassium 5.7 mEq per L, sodium 144 mEq per L, carbon dioxide combining power 47 volumes percent, chloride 110.6 mEq per L. An electrocardiogram was normal.

The patient seemed to improve while receiving only symptomatic therapy although she continued to regurgitate feedings. X-ray examination of the skull showed some bulging of the anterior fontanelle; the sutures were widened and there was an area of increased density in the parietal region of the vertex; examination of the bones of the upper and lower extremity showed marked periostitis with subperiosteal hemorrhage in the femora and tibiae, and to a lesser extent in the right humerus.

Because the x-rays and clinical picture were so suggestive of traumatic periostitis, and the vomiting continued, it was felt that a subdural hematoma might be present.

A subdural tap was done on April 21, and bloody fluid was obtained; 7 cc from the right side, 5 cc from the left side. This fluid contained protein 520 mg. per 100 ml., sugar 152 mg. per 100 ml., WBC 50, 80 percent of which were lymphocytes, RBC 80,000. Subdural punctures were repeated on April 22 and April 23 with essentially the same results. On April 25, a craniotomy for evacuation of the hematoma was performed.

DISCUSSION

Dr. Burke:

The x-rays of the skull show the sutures to be somewhat separated, and after one month of age this degree of separation, particularly of the squamosal suture, should be judged as evidence of possible increase in intracranial pressure. The fontanelle anteriorly is bulging; the lambdoidal and coronal sutures are quite widely spaced. One must be very careful about interpreting suture separation in a newborn baby, particularly with moulding because the edema of the scalp tissues may give a false impression of increased intracranial pressure. In breech deliveries, particularly of prematures, trauma to a baby's head is well known, and Matson and Ingraham's classical reviews of this subject point out that this is by far the commonest cause of subdural hematoma in infants.

Whether subclinical deficiencies of vitamins C, D or K during a mother's pregnancy may play a role in the etiology of subdural hematoma, one may only speculate. Similarly, subclinical degrees of vitamin C and D deficiency may influence the characteristic periosteal changes in the long bones. The

stresses and strains on bones in the normal handling of a baby frequently are sufficient to produce osteal and periosteal changes, although not necessarily to the degree that we see here. Possibly as high as 20 or 25 percent of premature babies will have tubular bone changes characterized by osteosclerosis and subperiosteal calcification. This is not entirely limited to premature babies, for periosteal trauma, characterized by subperiosteal calcification, is not uncommon in breech babies. I have seen several cases where the epiphysis of the femur has been actually dislocated and stripped during a difficult delivery of an aftercoming head, when considerable pressure was applied to the lower extremities. The lesions here are limited largely to the shafts and lower portions where the periosteum which is very pliable, particularly in the premature, pulls away from the cortex, and ruptures all of the periosteal vessels, with subsequent exudation of blood, which later organizes and calcifies. It is a surprisingly fast process; whereas a period of two to three weeks following injury is usually necessary for calcification to appear on the x-ray of the older child, calcification is visible by x-ray in small, newborn babies in five to seven days. Periosteal lifting all along the shaft and some periosteal accumulation of the blood which has subsequently calcified helps to distinguish this lesion from such things as syphilis or osteomalacia. Another feature in long bones in small babies is the sclerosing procedure that goes on in the cortex. The spongiosa is very much narrowed, and the cortex impinges upon the spongiosa and gives a localized condensation. This sign in premature babies is quite normal, and even in the first two or three weeks of life, thickening of the cortex with narrowing of the spongiosa is not an abnormal sign.

Elevation of the periosteum with subperiosteal calcification must be evaluated as being mild or excess, since mild to moderate degrees of periosteal elevation without fracture or massive subperiosteal calcification are not uncommon and are quite normal.

I think Dr. LoPresti saw these symptoms and signs, recognized them as characteristic of traumatic periosteal reaction, and remembered the association that Dr. Caffey has made that with such babies one should always think of subdural hematoma. These injuries to bone are characterized by no untoward residuals.

It is more characteristic, I think, to find this sort of injury in babies where the rate of growth is rapid, for example in premature babies. Bigger babies who are subject to trauma during delivery are more likely to receive fracture rather than periosteal stripping.

Dr. Maynard Cohen:

This case has been very interesting to me because although similar patients may have been seen in the hospital, this is the first case with such

advanced signs that I have seen myself. Actually, when the baby was admitted to the hospital she must have appeared acutely ill because the house staff saw fit to place her in an oxygen tent. I saw her the morning following admission at which time she was undoubtedly more comfortable. The most striking finding upon examination was the swelling involving the right thigh, which was smooth and firm, somewhat tender, and possibly a little bit warm. Some of the obvious causes were thought of and subsequently dismissed in the next few days; the possibility of a suppurative lesion, syphilis or rheumatic fever and various other diseases which are extremely unlikely in this age group, were not seriously considered. The blood studies and, of course, subsequently the x-ray examinations were very enlightening.

The history reveals the nature of the delivery, but one item that appears in the record but not in the above summary should be stressed. The baby's legs were x-rayed by the obstetrical service after she was delivered, presumably because it was felt that this was a somewhat traumatic delivery. Apparently those x-rays were reported as normal, and that might very well be expected since no changes of this nature would appear for at least an interval of one week, as Dr. Burke has said. The possible contributing

FIG. 1. X-ray examination of the bones of the lower extremities reveals marked periostitis with sub-periosteal hemorrhage in the femora and tibiae. While lues must be considered traumatic periostitis is the most likely diagnosis.

factor of poor nutrition mentioned by Dr. Burke interests me too. The baby's history states that she had eaten well but had not retained feedings. One other note indicated that the baby had not received vitamin D; it is probably safe to assume she had not received vitamin C either. Although a clearcut picture of scurvy may not appear until two or three months of age, I would think subclinical scurvy could be a contributing factor to the hemorrhage. Should patients of this nature appear again, vitamin C studies might be done before vitamins and other hospital therapy are instituted.

Initially, the subdural hematoma was not suspected, and it really was not thought of for a period of a few days. In retrospect however, the long history of poor development, vomiting and irritability, and the poor status of the child, should have suggested it immediately.

Dr. LoPresti:

I would like to say a few words to complete the picture. A group of us went down to the x-ray department to review the films on this patient, and it was recognized, as it had been reported by the x-ray department, that this represented traumatic periostitis. As a method o teaching we turned to Caffey's "Pediatric X-Ray Diagnosis". He states that his clinic had pointed out the frequent association of subdural hematoma with traumatic periostitis in newborn infants. At that point everything fell into place, and we did subdural taps which produced bloody fluid. We are going to send a little note to Dr. Caffey thanking him for making the diagnosis for us.

As Dr. Burke has so well illustrated, traumatic periostitis is not well publicized and this is the main purpose of presenting our patient today. It occurs rather commonly, and if suspected should be diagnosed more frequently. It is important to note that traumatic periostitis occurs not only as the result of obstetrical trauma, but also may occur following injury in any of the infant age levels, because in infancy the periosteum is extremely vascular and quite loosely attached to bone. Dr. Burke has touched upon one important factor in this condition, namely, that frequently a history of trauma is absent in these infants. Perhaps the parents are reluctant to discuss the possibility that trauma has occurred; or since the x-ray changes are seen two or three weeks after the injury, the initial trauma may have been forgotten. For these reasons when the child is x-rayed, and the marked periosteal reaction is seen, (and it may be unilateral or bilateral, and/or monostotic or polyostotic), one may suspect a condition which is much more serious than traumatic periostitis. The radiologist and other physicians dealing with such infants often will suspect diseases such as syphilitic periostitis, osteomyelitis, or tuberculosis; and in a few of the reported cases, even the possibility of malignant disease. This fact makes traumatic periostitis a relatively important problem, and one which should be recognized

more frequently. It should be considered even in children where the history of trauma is absent initially, because in going back over the history one can usually elicit some evidence of trauma. Again I would like to point out that traumatic periostitis occurs not only in newborn infants as a result of obstetrical trauma but also in any infant whose extremities are subjected to trauma. Dr. Mateos performed the operations on this patient and I have asked him to come and say a few words about subdural hematoma, and the surgical procedures performed on our patient.

Dr. Mateos:

The observation that traumatic periostitis is often associated with subdural hematomas seems most logical since the dura is the periosteum of the bones of the skull and it is the bleeding of the vessels of the dura that produces the subdural hematomas. When the small veins that course between the dura and the brain are torn, the collection of blood under the dura breaks down chemically, and a membrane develops around a pocket of high protein fluid. This causes the osmotic absorption of spinal fluid into it and increases the size of the sac and therefore the intracranial pressure. This infant was tapped subdurally and bloody fluid was obtained bilaterally; on repeated taps there was a very yellow fluid with high protein content. We felt that an operation should be performed to remove the membrane. There are different ways of handling these cases; some neurosurgeons prefer to do repeated taps before craniotomy; some do burr holes first, and only if this reveals a membrane, do a craniotomy. We feel that since craniotomy in children is such a simple procedure and such a great percentage of children have a membrane, it is far better, instead of two operations (burr holes first and then craniotomy) to do the craniotomy in the first instance. The procedure must be done bilaterally; the results are better when at least ten days intervene between the two sides. In this patient we found the membranes on both sides.

Lately, at Johns Hopkins University Hospital, there have been some studies wherein radioactive phosphorus has been injected intravenously and then recovered from subdural effusion. With this procedure one can determine whether a membrane-enclosed sac or just a simple effusion exists, because in an effusion they can recover greater amounts of radioactive phosphorus more quickly.

We feel that this child is going to have good recovery because of the complete removal of the membranes.

Dr. LoPresti:

Before the first craniotomy was performed this patient failed to gain weight, continued to vomit and looked as if she were going downhill even

in the hospital. Since the surgery she is doing very nicely; the vomiting has ceased; and we believe that we have effected a cure.

Dr. Stevens:

I wonder if the etiology of this syndrome has not been a little oversimplified, and with too much emphasis on trauma. As you know we have found a good many patients with subdural effusions who never had trauma, who never had had meningitis, but did have diarrhea. I wonder what the sequence is in this child. Does the subdural hematoma produce the usual sequence of nausea, vomiting, anorexia, and dehydration, or is it the other way around? Is the subdural effusion there from birth? The other point that has not been mentioned so far is that this syndrome occurs in older children of ages 2 and 3 years, in well nourished children and with no history of trauma. Of course we always question the history from the parents and may even question their motives regarding trauma. However, there have been too many cases of this syndrome, too many of them well documented with no evidence of trauma. There must be more to it than trauma. One of the most convincing demonstrations of this is the fact that subdural hematoma may occur in children who not only have periostitis but also multiple fractures, and the fractures are not only in the long bones but may be in the scapula and the ribs as well.

The other possibility of course is that there is more than one cause. For example, there have been several cases reported in which there was not a vitamin C deficiency as there may have been in this case, but rather excessive vitamin A intake. At least two such cases have been reported. In one case that I saw, the child was given viosterol, one teaspoonful a day instead of several drops, with an eventual x-ray picture that looked like leutic periostitis. I do not believe we have the complete answer for subdural hematomas yet.

VIRUS DIARRHEA

Journal Club Review

E. Ahrens, M.D.*

INTRODUCTION

At present remarkably little is known of the role of viruses in infectious diarrheas of the infant and child. Excellent bacteriological techniques are readily available for the determination of pathogenic bacteria in cases of diarrhea. Unfortunately, in the majority of such cultures no bacterial

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pathogen can be isolated. In one series of 518 children with diarrhea it was observed that only 4.4 percent had a bacterial enteric infection, 40 percent had parenteral infections, and 55.6 percent had "suspected enteric infections"[1].

The clinician often suspects that pathogenic viruses cause this large group of "suspected enteric infections". As of the present, however, his suspicion has not been confirmed in the laboratory. The techniques, the equipment, the culture media and animals, and the trained personnel for viral identification are not yet available, except in a few research centers.

It is probable that in the future only a small group of viruses will be found to be causative of diarrhea in infants. Other viruses may prove to be an associated finding or to produce diarrhea only in the particularly susceptible individual, e.g., the newborn.

As is well known, many viruses do not produce diarrhea. The common cold is usually characterized by constipation. The common exanthems and poliomyelitis are rarely associated with diarrhea, although the specific viruses can be cultured from the stool. Rabies and the viral encephalitides also are not commonly associated with diarrhea[1].

Observation Of Viral Diarrhea In Animals

Much of the early research on viral diarrhea was devoted to studies of naturally occurring and experimentally produced diarrhea in animals.

An important step in the knowledge of viral diarrhea was the research devoted from 1928–1943 to infectious panleukopenia of cats. This is a natural disease of cats in which diarrhea is a major symptom. A filtrable agent was finally established as the pathogen[2], and was one of the first viruses to be implicated as a cause of diarrhea in an animal.

In 1942 a filtrable agent was isolated by Baker in a natural disease of calves characterized by diarrhea, pneumonia, and fever. Inoculation of this agent would produce the same syndrome in other calves and in mice would produce pneumonia[2].

In 1948 an endemic diarrhea in suckling mice was described. Cytoplasmic inclusion bodies were found in the epithelium of the small intestine of the affected animals. Transmission of the disease was demonstrated with bacteria free filtrates of this intestine[2].

In 1954 Baker described a calf diarrhea with fever, leukopenia, and diarrhea. He was able to infect other calves and observed the development of immunity to future infections. An attenuated filtrable agent was produced by repeated rabbit transfers which gave only minor symptoms on inoculation and yet gave full immunity to the virulent strain of this virus[3].

Observation Of Viral Diarrhea In Adults

Several studies have been carried out in which a filtrable agent was transmitted from infected humans to healthy volunteers with production of

clinical syndromes including diarrhea. In neither of the following studies, however, was the viral agent isolated, cultivated, or given to experimental animals.

In 1944 the virus of infectious hepatitis was given by duodenal drainage to volunteers and subsequent diarrhea was frequently observed[1]. In 1947 a highly contagious epidemic of gastroenteritis of adults with symptoms of lowgrade fever, malaise, nausea, vomiting, and diarrhea was carefully studied by Gordon, Ingraham, and Korns. They made passages of the infection with bacteria free filtrates from human to human and observed the development of neutralizing antibodies in convalescent serum[4].

Observation Of Viral Diarrhea In Infants And Children

As early as 1944 Buddingh and Dodd reported a syndrome of an unusual stomatitis often associated with diarrhea[5, 6, 7]. They noted that diarrhea was the more prominent symptom under the age of 6 months, and stomatitis was the major or only feature in older children and adults. The infection was of short duration and highly contagious. In their series the infecting virus produced diarrhea in ⅓ of the patients and stomatitis in ¾ of the patients. The stomatitis was commonly localized to the anterior tip and under-surface of the tongue, the gums, and the inner aspect of the lip. The lesions were small vesicles persisting only 24 hours followed by excoriations of the mucosa[5].

Stool and mouth cultures of infected infants and attending nursing personnel were filtrated and inoculated in young rabbit cornea. Initially, rabbit cornea was used to determine if this was an unusual form of herpetic stomatitis. Instead of the expected herpetic inclusion body reaction of the rabbit cornea, a characteristic gross and microscopic sequence of corneal changes was observed that proved to be typical and to the investigators diagnostic of the syndrome. The agent could be propagated and maintained in serial transfer on rabbit corneas and could be filtered[5].

In the hands of these investigators, cultures from cases of moniliasis, "Vincent's" stomatitis, and from the mouth and stool of well infants did not produce the characteristic destructive and inflammatory response of the rabbit cornea. There were no intranuclear or intracytoplasmic inclusion bodies observed. Transmission to other types of animals or to egg embryo cultures proved impossible[6].

The belief that this corneal reaction was a specific viral reaction was reinforced by the following observations:

a) Immunity in an inoculated rabbit eye occurred 3 weeks after initial inoculation and thereafter no characteristic corneal reaction could be produced; and b) as of 1957 mouth and stool sample filtrates isolated in infant epidemic diarrheas of Memphis, Cincinnati and Boston showed a cross immunity in the rabbit cornea with the virus of Nashville[7].

The investigators had observed that the nursing personnel during epidemics of infant diarrhea frequently were asymptomatic or had only a mild stomatitis. Nevertheless, their mouth and stool filtrates when inoculated gave characteristic rabbit corneal reactions. Stimulated by the appearance of diarrhea in infants as young as 3 days old, cultures were taken of the mothers of some of the infected infants with remarkable results. In one epidemic 10 mothers and infants were examined; samples of 8 mothers and 7 infants gave characteristic corneal reaction, although all of the mothers were asymtomatic[6].

Cummings has been unable to confirm the work of Buddingh and Dodd. In an extensive study of epidemic diarrhea of the newborn he considered the rabbit corneal reaction to prove quite non-specific. Fifteen hundred rabbit corneas were inoculated or traumatized with many different agents and all gave corneal reactions similar to those described by Buddingh and Dodd[8].

In another infantile diarrhea study Light & Hodes were encouraged by Baker's studies of diarrhea of the young calf. After failing in two epidemics to produce diarrhea in a variety of animals, they attempted to inoculate young calves with stool filtrates, nasal secretions, and blood samples of infants with epidemic diarrhea of the newborn. In four subsequent epidemics the calf, as an experimental animal, was used with consistent success[2, 9].

The infant samples were filtered and inoculated intranasally or subcutaneously into calves with production of bloody mucoid diarrhea within 2 days. Successive passages were performed with bacteriologically sterile filtrates in calves.

Characteristically the infants were under 6 weeks of age, had no enteric bacterial pathogens demonstrable, had no stomatitis, and were equally affected whether bottle or breast fed[2].

The investigators were careful to observe that this agent differed from Baker's studies in that no pneumonia or high fever was noted in calves, and no pneumonia could be produced in mice. As a further control, scours, a diarrheal disease common to calves, was considered but noted to be clinically different. Also scours could not be inoculated to produce calf diarrhea. Stools of normal infants and stools of normal calves could not produce the syndrome[2].

Attempts to protect unexposed calves by passive immunization with convalescent infant sera gave complete protection to 2 calves and partial protection to 2 calves. There was cross immunity for calves. Older calves tended to have milder diarrhea.

Cummings verified the work of Light & Hodes in his survey of infantile diarrhea. His group also found that of a wide variety of animals inoculated with specimens from infected infants, only the newborn or young calf

developed diarrhea. He confirmed that a watery diarrhea could be produced in calves from infected infant samples, that passages were possible, that the agent was Seitz filtrable, and that the agent could be separated from bacteria by ultracentrifugation[8].

A third and more recent study of infantile diarrhea is of note though by no means conclusive. Ramos-Alvarez cultured 56 children under the age of 4 years with undifferentiated diarrheal syndromes for virus in the summer of 1955. Cytopathogenic agents were recovered from 24 of the 56 rectal cultures in monkey kidney tissue. Suckling mice and immunologic studies indicated additional viral infections in some of the negative monkey tissue cultures. Viral infections were considered present in 55 percent of the group. Among the viruses were Poliomyelitis, Coxsackie, and Enteric Cytopathogenic Human Orphan virus. There were in addition 12 viral types that could not be classified with any of the pooled antisera that were available[10].

This study does not mention the production of diarrhea in animals. One may question whether the viruses isolated are merely associated findings or are pathogenic agents. Nevertheless, such reports of viral cultures of non-specific diarrheas constitute a further step in the effort to clarify the role of virus in infant diarrhea.

SUMMARY

A brief resume of recent studies of animal and human viral diarrheas has been given.

There is no question but that some viruses can produce diarrhea in the susceptible individual while others do not. It has been observed that the very young animal or infant may respond to a viral infection with diarrhea as the major symptom, whereas the older individual may have other symptoms or no symptoms. This diarrhea, whether bacterial or viral, is of greatest significance in the care of the newborn and especially of the premature infant because of the potential threat to life.

Over one-half of diarrheas in children are non-specific. In at least one study over one-half of the non-specific diarrhea stools contained viruses which may be merely an associated finding or may at later date be determined as the causative agent of that diarrhea.

There is a great need for newer and simpler methods of isolating and culturing viruses and then making such laboratory aids more widely available.

Present viral studies suggest that either the mother at birth or the nursing personnel after birth may be the asymptomatic carrier of a pathogenic virus producing epidemic diarrhea of the newborn.

There is at the present time no substitute for basic principles of good nursery care to prevent or control epidemic infant diarrhea.

In the older infant or child, intelligent fluid and electrolyte management and good isolation technique continue to be of primary concern in giving the best possible care to the non-specific diarrhea patient.

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SUGGESTED ORAL DAILY DOSAGE†

0 to 3 years	10 to 40 mg.
3 to 6 years	20 to 60 mg.
6 to 12 years	40 to 120 mg.
Adults	50 to 200 mg.

†Colace may be given in divided doses. The higher dosage is recommended during initial phase of therapy. Dosage should be adjusted as required by individual response.

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